

sequences derived from at least three homologous genes, and

(b) wherein said cleavage sites are unique within each gene sequence,

(bb) do not form compatible sites with respect to any single sub-sequence, and

(bc) are common to all homologous sub-sequences.

61. (Amended) A kit comprising a collection of (poly) peptides according to claim 60 and suitable host cells therefor.

Please add the following new claims:

62. A synthetic antibody molecule comprising a variable heavy chain polypeptide sequence and a variable light chain polypeptide sequence, wherein each of said variable polypeptide sequences comprise four framework regions and three complementarity determining regions, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of a sequence selected from the group consisting of VH1A (SEQ ID NO:57), VH1B (SEQ ID NO:59), VH2 (SEQ ID NO:61), VH3 (SEQ ID NO:63), VH4 (SEQ ID NO:65), VH5 (SEQ ID NO:67), and VH6 (SEQ ID NO:69), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of a sequence selected from the group consisting of V $\kappa$ 1 (SEQ ID NO: 43), V $\kappa$ 2 (SEQ ID NO: 45), V $\kappa$ 3 (SEQ ID NO: 47), V $\kappa$ 4 (SEQ ID NO: 49), V $\lambda$ 1 (SEQ ID NO: 51), V $\lambda$ 2 (SEQ ID NO: 53), and V $\lambda$ 3 (SEQ ID NO: 55).

63. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding

framework regions of VH1A (SEQ ID NO:57), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V<sub>κ</sub>1 (SEQ ID NO: 43).

64. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1A (SEQ ID NO:57), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V<sub>κ</sub>2 (SEQ ID NO: 45).

65. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1A (SEQ ID NO:57), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V<sub>κ</sub>3 (SEQ ID NO: 47).

66. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1A (SEQ ID NO:57), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V<sub>κ</sub>4 (SEQ ID NO: 49).

67. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1A (SEQ ID NO:57), and wherein the four framework

regions of said variable light chain comprise the corresponding framework regions of V $\lambda$ 1 (SEQ ID NO: 51).

68. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1A (SEQ ID NO:57), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\lambda$ 2 (SEQ ID NO: 53).

69. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1A (SEQ ID NO:57), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\lambda$ 3 (SEQ ID NO: 55).

70. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1B (SEQ ID NO:59), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\kappa$ 1 (SEQ ID NO: 43).

71. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1B (SEQ ID NO:59), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of

V<sub>K</sub>2 (SEQ ID NO: 45).

72. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1B (SEQ ID NO:59), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V<sub>K</sub>3 (SEQ ID NO: 47).

73. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1B (SEQ ID NO:59), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V<sub>K</sub>4 (SEQ ID NO: 49).

74. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1B (SEQ ID NO:59), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V<sub>λ</sub>1 (SEQ ID NO: 51).

75. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1B (SEQ ID NO:59), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V<sub>λ</sub>2 (SEQ ID NO: 53).

76. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH1B (SEQ ID NO:59), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\lambda$ 3 (SEQ ID NO: 55).

77. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH2 (SEQ ID NO:61), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\kappa$ 1 (SEQ ID NO: 43).

78. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH2 (SEQ ID NO:61), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\kappa$ 2 (SEQ ID NO: 45).

79. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH2 (SEQ ID NO:61), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\kappa$ 3 (SEQ ID NO: 47).

80. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH2 (SEQ ID NO:61), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\kappa$ 4 (SEQ ID NO: 49).

81. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH2 (SEQ ID NO:61), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\lambda$ 1 (SEQ ID NO: 51).

82. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH2 (SEQ ID NO:61), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\lambda$ 2 (SEQ ID NO: 53).

83. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH2 (SEQ ID NO:61), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\lambda$ 3 (SEQ ID NO: 55).

84. The synthetic antibody molecule according to claim 62, wherein the four

framework regions of said variable heavy chain comprise the corresponding framework regions of VH3 (SEQ ID NO:63), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\kappa$ 1 (SEQ ID NO: 43).

85. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH3 (SEQ ID NO:63), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\kappa$ 2 (SEQ ID NO: 45).

86. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH3 (SEQ ID NO:63), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\kappa$ 3 (SEQ ID NO: 47).

87. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH3 (SEQ ID NO:63), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\kappa$ 4 (SEQ ID NO: 49).

88. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding

framework regions of VH3 (SEQ ID NO:63), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\lambda$ 1 (SEQ ID NO: 51).

89. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH3 (SEQ ID NO:63), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\lambda$ 2 (SEQ ID NO: 53).

90. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH3 (SEQ ID NO:63), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\lambda$ 3 (SEQ ID NO: 55).

91. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH4 (SEQ ID NO:65), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\kappa$ 1 (SEQ ID NO: 43).

92. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH4 (SEQ ID NO:65), and wherein the four framework regions

of said variable light chain comprise the corresponding framework regions of  $V_{\kappa 2}$  (SEQ ID NO: 45).

93. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of  $VH4$  (SEQ ID NO:65), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of  $V_{\kappa 3}$  (SEQ ID NO: 47).

94. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of  $VH4$  (SEQ ID NO:65), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of  $V_{\kappa 4}$  (SEQ ID NO: 49).

95. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of  $VH4$  (SEQ ID NO:65), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of  $V_{\lambda 1}$  (SEQ ID NO: 51).

96. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of  $VH4$  (SEQ ID NO:65), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of  $V_{\lambda 2}$

(SEQ ID NO: 53).

97. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH4 (SEQ ID NO:65), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\lambda$ 3 (SEQ ID NO: 55).

98. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH5 (SEQ ID NO:67), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\kappa$ 1 (SEQ ID NO: 43).

99. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH5 (SEQ ID NO:67), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\kappa$ 2 (SEQ ID NO: 45).

100. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH5 (SEQ ID NO:67), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\kappa$ 3 (SEQ ID NO: 47).

101. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH5 (SEQ ID NO:67), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\kappa$ 4 (SEQ ID NO: 49).

102. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH5 (SEQ ID NO:67), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\lambda$ 1 (SEQ ID NO: 51).

103. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH5 (SEQ ID NO:67), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\lambda$ 2 (SEQ ID NO: 53).

104. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH5 (SEQ ID NO:67), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\lambda$ 3 (SEQ ID NO: 55).

105. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH6 (SEQ ID NO:69), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\kappa$ 1 (SEQ ID NO: 43).

106. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH6 (SEQ ID NO:69), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\kappa$ 2 (SEQ ID NO: 45).

107. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH6 (SEQ ID NO:69), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\kappa$ 3 (SEQ ID NO: 47).

108. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH6 (SEQ ID NO:69), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\kappa$ 4 (SEQ ID NO: 49).

109. The synthetic antibody molecule according to claim 62, wherein the four

framework regions of said variable heavy chain comprise the corresponding framework regions of VH6 (SEQ ID NO:69), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\lambda$ 1 (SEQ ID NO: 51).

110. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH6 (SEQ ID NO:69), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\lambda$ 2 (SEQ ID NO: 53).

111. The synthetic antibody molecule according to claim 62, wherein the four framework regions of said variable heavy chain comprise the corresponding framework regions of VH6 (SEQ ID NO:69), and wherein the four framework regions of said variable light chain comprise the corresponding framework regions of V $\lambda$ 3 (SEQ ID NO: 55).

112. An immunoglobulin polypeptide comprising four amino acid consensus framework sub-elements and having interspaced complementarity determining region (CDR) sub-elements, wherein said polypeptide is produced by the steps of: (i) aligning a plurality of known human immunoglobulin sequences; (ii) identifying the conserved framework sub-elements of said known and aligned human immunoglobulin sequences; (iii) comparing amino acids at each corresponding position of said conserved framework sub-elements; (iv) deducing consensus sequences for the framework sub-elements based on said comparing step (iii); (v)

synthesizing a nucleic acid molecule capable of encoding said polypeptide, wherein said nucleic acid molecule comprises DNA cleavage sites at the boundary between each consensus framework sub-element and CDR sub-elements; and (vi) allowing the expression of said synthesized DNA molecule as said immunoglobulin polypeptide.

113. The immunoglobulin polypeptide according to claim 112, wherein said plurality of known human immunoglobulin sequences are human V<sub>k</sub> immunoglobulin sequences.

114. The immunoglobulin polypeptide according to claim 112, wherein said plurality of known human immunoglobulin sequences are human V<sub>λ</sub> immunoglobulin sequences.

115. The immunoglobulin polypeptide according to claim 112, wherein said plurality of known human immunoglobulin sequences are human V<sub>H</sub> immunoglobulin sequences.